Guideline for the management of Unconjugated Hyperbilirubinaemia

Over the past 20 years there has been a change in the management of jaundice to a more “kinder and gentler approach”, following concerns that previously management was too aggressive.

Most babies have a transient rise in serum bilirubin following birth with nearly all preterm babies becoming jaundiced and about 50% of term neonates developing jaundice. If jaundice is not recognised and treatment not started promptly, kernicterus may develop. Kernicterus is a rare complication that occurs when bilirubin is deposited in brainstem nuclei which can result in athetoid cerebral palsy.

Investigation and management of jaundice is influenced by many factors including maternal details such as blood group and ethnicity, gestation, condition of the infant and timing of onset of jaundice. Jaundice that presents in the first 24 hours of life is considered pathological, if presentation is within days 2 -7 it is often physiological and if prolonged (>14 days in term infants) always requires investigation (please refer to the Guideline on the management of prolonged jaundice). The most common causes for hyperbilirubinaemia include prematurity, rhesus or ABO incompatibility, sepsis, significant bruising/IVH, dehydration and/or poor feeding.

Below is a list of symptoms, signs and investigations that suggests the jaundice requires further investigation and treatment:

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Biochemical / Haematology</th>
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<tbody>
<tr>
<td>Onset in the first 24 hrs</td>
<td>Cord Haemoglobin &lt; 120g/L</td>
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<tr>
<td>Vomiting, poor feeding</td>
<td>Cord Bilirubin &gt;60µmol/l</td>
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<td>Irritability, high pitched crying</td>
<td>Cord Direct Coombs Test (DCT) strongly +ve</td>
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<tr>
<td>Fever, lethargy</td>
<td>Haemoglobin &lt; 12g/dl</td>
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<tr>
<td>Bilirubin rising &gt;10µmol/l/hr</td>
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Babies at high risk for significant hyperbilirubinaemia:

- Babies less than 38 weeks.
- Previous sibling requiring phototherapy.
- Visible jaundice within the first 24 hours

Management Principles:

1. If jaundice is suspected within 24 hours of birth, document both maternal and neonatal Blood Groups, Rhesus status and if there is incompatibility check the DCT. Check bilirubin levels 4-6 hourly until the rate of rise is known. Assess ethnicity, as G6PD deficiency has a higher incidence in neonates of Mediterranean, Asian and African extraction. Family history should be sought for haemolytic/haematological diseases (spherocytosis), or jaundice in previous siblings. Ask about the feeding history and assess whether the neonate is dehydrated. Examine carefully looking for signs of sepsis.
   - If the mother is Rhesus –ve, cord blood for FBC, DCT and bilirubin should be sent by the midwife from Labour Ward.
   - First line Investigations should include Blood group, Rhesus status, FBC, blood film, urea and electrolytes and serum bilirubin.
   - Consider doing a partial septic screen and G6PD levels and blood film.

When measuring jaundice do not rely on direct inspection alone as this can easily underestimate jaundice levels. When inspecting, check the baby in bright and preferably natural light. Examination of sclera, gums and blanched skin is useful in neonates of all skin tones. Where jaundice is suspected a formal measurement (transcutaneous or serum) should be performed.

2. Measuring Bilirubin:
   - Transcutaneous Bilirubinometers may be used in babies over 35 weeks with jaundice detected after 24 hours.
   - Serum bilirubin should be used if transcutaneous reading is above 250micromol/litre.
   - If a baby has been or is on phototherapy then serum bilirubin levels should be used.
   - Serum bilirubin should be measured in all babies less than 35 weeks.
   - Serum bilirubin levels should also be measured in all babies with who are jaundice at less than 24 hours.
   - Measurements of transcutaneous bilirubin levels should be from the forehead or sternum and should be a best of three values.
3. **Feeding and Hydration**: Dehydration is known to exacerbate hyperbilirubinaemia. Aim for good hydration with oral feeds preferably breast milk, if breast/bottle feeds are not tolerated give milk via NG tube and if necessary start IV fluids.

4. **Phototherapy**: is a safe and convenient way of lowering serum bilirubin and it reduces the need for exchange transfusions. Plot the serum bilirubin on the appropriate graph for gestation (see link at bottom of page), and insert the graph in the notes and start phototherapy accordingly. Expose as much surface area of the baby as possible to the phototherapy especially if the bilirubin is approaching exchange level. Consider increasing to double or triple phototherapy if the bilirubin is high or close to the exchange line (e.g. use a bili-blanket as well as on overhead light). Unless there are signs of dehydration there is no need for routinely increasing the fluid intake once phototherapy is initiated. Phototherapy does not need to be continuous and may be interrupted briefly for cares, parental visits and for feeds. Check the serum bilirubin 4-12 hourly once phototherapy has started and 6-12 hours after stopping to look for rebound hyperbilirubinaemia. Phototherapy should be stopped once bilirubin levels greater than 50 µmol/l below treatment threshold. Prophylactic phototherapy is of no benefit even for preterm or VLBW neonates.

5. **Exchange Transfusion**: is now performed infrequently compared with 20 years ago and has an associated significant morbidity and mortality of 0.3%. The decision to perform one is always a consultant decision. (Please see the practical guideline on how to perform an exchange transfusion in the guideline folder). Exchange transfusions remain necessary for neonates that fail to respond to phototherapy especially if the bilirubin level is rising >10µmol/l/hr (bilirubin should decrease by 8-17µmol/l/hour once phototherapy initiated) and those that present late with a bilirubin level higher than a given exchange value. There is no benefit in giving albumin to decrease unbound bilirubin unless serum albumin is <30g/l. If jaundice is due to haemolysis high dose IV immunoglobulin should be considered as it reduces the need for exchange transfusion, but increases the rate of late top-up transfusions. The dose for IVIG is shown below.

IVIG dose (preparation VIGAM) = 500mg/kg given over 4 hours.

**Preterm infants**
Any preterm infant that becomes jaundiced within 24 hours of birth should start phototherapy. Above 72 hours the following formula can be used to calculate phototherapy threshold. (Bilirubin levels should always be plotted on chart.)

Bilirubin (micromol/litre) = (gestational age × 10) – 100

An **exchange transfusion** should be performed if the rate of bilirubin rise is >8.5µmol/l/h despite phototherapy or if bilirubin levels exceed treatment thresholds on charts. A guide to treatment threshold can be calculated as below.

Bilirubin (micromol/litre) = gestational age × 10 (can be used from 72 hours, before 72 hours see treatment graph)

**Term infants**
Healthy term neonates (≥37 weeks) tolerate higher levels of bilirubin compared with preterms or sick neonates. However, jaundice in the first 24 hours, bilirubin ≥200µmol/l at 48 hours, bilirubin ≥250µmol/l at 72 hours or ≥350µmol/l at 96 hours is worrying and should be investigated and treated.

**Exchange transfusion** should be considered with bilirubin levels of >100 at birth, >200 at 24 hours and >450 from 42hours.

**NICE jaundice guideline**

**References**
Rennie JM. Robertson's Textbook of Neonatology 4th ed
AAP clinical practice guideline. Management of hyperbilirubinaemia in the newborn infant 35 weeks or more weeks of gestation. Pediatrics 2004;114:1
Dr.Gupta, Dr Sybil Barr September 2014 (to be updated September 2017)